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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ROONEY, NORA MAUREEN	
ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,052	FERREIRA ET AL.	
	Examiner	Art Unit	
	NORA M. ROONEY	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-18 and 20-40* is/are pending in the application.

4a) Of the above claim(s) *5-14,16,17 and 21-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-4, 15, 18, 20, 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and declaration of Fatima Ferreira filed on 12/03/2007 are acknowledged.

2. Claims 1, 3-18 and 20-40 are pending.

3. Claims 5-14, 16-17 and 21-37 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 06/01/2007.

4. Claim 1, 3-4, 15, 18, 20 and 38-40 are currently under examination as they read on a polypeptide of SEQ ID NO:1 and a kit thereof.

5. The following rejections are necessitated by Applicant's amendment filed on 10/03/2007.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 3-4, 15, 18, 20 and 38-40 *are* rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: an allergen consisting of SEQ ID NO:1; a polypeptide consisting of amino acids 181 to 396 of SEQ ID NO:1 and a polypeptide consisting of amino acids 21 to 180 of SEQ ID NO:1, a composition comprising the allergen and a kit thereof, does not provide reasonable enablement for: an isolated allergen consisting of a polypeptide capable of binding to IgE antibodies from an individual being allergic against mugwort pollen, wherein said polypeptide is selected from the group consisting of : (a) **a polypeptide having an amino acid sequence that is at least 95% identical to the amino acid sequence as shown in SEQ ID NO: 1**; (b) **a polypeptide comprising the amino acid sequence extending between residues 21 and 180 of SEQ ID NO:1**; and (c) **a polypeptide comprising the amino acid extending between residues 181 and 396 of SEQ ID NO:1 of claim 1**; wherein said polypeptide **comprises** the amino acid sequence as shown in SEQ ID NO: 1 of claim 3; wherein said polypeptide is further **capable of binding to IgE antibodies from an individual being allergic against ragweed pollen** of claim 4; A **pharmaceutical composition** comprising the allergen as claimed in any one of claims 1, 3 or 4 of claim 15; A kit for the diagnosis, treatment or **prevention** of an allergic disorder comprising the allergen as claimed in any one of claims 1, 3 or 4 of claim 18; the allergen of claim 3, wherein the polypeptide is further **capable of binding to IgE antibodies from an individual being allergic against ragweed pollen** of claim 20; wherein said polypeptide consists of the amino acid sequence as shown in SEQ ID NO:1 of claim 38; wherein said polypeptide consists of the amino acid sequence extending between residues 21 and 180 of SEQ ID NO:1 of claim 39; and wherein said polypeptide consists of the amino acid sequence extending between residues 181 and 396 of SEQ

ID NO:1 of claim 40. The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

On pages 14-20 of the specification, Applicant discloses the purification, screening, cloning, sequencing and recombinant expression of the 40.9 kDa mugwort pollen allergen of SEQ ID NO:1. Sera from mugwort allergic patients were also tested for reactivity to the 40.9 mugwort pollen allergen in vitro.

Applicant has not adequately disclosed an allergen consisting of a polypeptide comprising a fragment of SEQ ID NO:1 or "an" amino acid sequence of SEQ ID NO:1 which reads on any two or more amino acid fragment of SEQ ID NO:1. Further, the term "comprising" opens up the claimed polypeptide to encompass any number of undisclosed amino acids added onto the N- and/or C- terminus of the peptide of SEQ ID NO:1. Therefore, the allergenic properties of the polypeptide maybe due to the additional undisclosed amino acid sequence and not to the peptide of SEQ ID NO:1 at all. Further, the specification fails to provide which core

structures of SEQ ID NO:1 are essential for IgE binding. Given the lack of sufficient guidance and predictability in determining IgE binding, it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of the claimed invention. Blumenthal et al. (PTO-892, Reference U) teaches that correlations between structure and IgE binding (or the lack of IgE binding) cannot be predicted on an a priori structural basis (In particular, entire document and page 39 of third full paragraph). Skolnick et al. (PTO-892, Reference V) teaches that sequence-based methods for function prediction are inadequate and knowing a protein's structure, i.e., amino acid sequence, does not necessary tell one its function (In particular, abstract, entire document). Attwood et al. (PTO-892, Reference W) teaches that protein function is context-dependent and the state of the art of making functional assignments merely on the basis of some degree of similarity between sequences and the current structure prediction methods is unreliable (In particular, entire document). Given the lack of guidance as to which specific amino acids within the polypeptide of SEQ ID NO:1 bind IgE and which amino acids can be added that also might bind IgE, it is unpredictable which polypeptide would exhibit the characteristics of an allergen with IgE binding. Absent the ability to predict which of these polypeptides would function as claimed, and given the lack of data on regions critical for activity, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

The Examiner does not know whether or not the claimed allergen polypeptide would function as pharmaceutical composition. In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the pharmaceutical composition

as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed pharmaceutical composition is effective for in vivo use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed pharmaceutical composition with a reasonable expectation of success.

Further at issue is whether or not the claimed method would function to "prevent" allergy. The specification provides no in vivo data to support the claimed subject matter. The specification fails to provide guidance as to how to totally prevent (100% prevention) allergy using a kit with the composition comprising a peptide of 18 or more consecutive amino acids of SEQ ID NO:1. The invention may reduce the likelihood of an allergy by administering the compound of SEQ ID NO:1, 3, 4 or 5, but the specification does not disclose how to totally prevent allergy. Therefore, the specification does not provide sufficient guidance on how to sufficiently prevent the occurrence of allergy by administering the claimed compound.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicant's arguments filed on 12/03/2007 have been fully considered, but are not found persuasive.

Applicant argues:

"Claims 1-4, 15, and 18-20 stand rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement. According to the Examiner, while the specification is enabling for an allergen consisting of SEQ ID NO: 1, it does not reasonably provide enablement for: (a) an allergen consisting of a polypeptide fragment comprising at least 18 consecutive amino acids from SEQ ID NO:l; (b) an allergen consisting of a polypeptide fragment capable of binding to IgE antibodies from individuals allergic to mugwort or ragweed pollen; (c) an allergen comprising the amino acid sequence of SEQ ID NO: 1; (d) a pharmaceutical composition comprising polypeptides as claimed; or (e) a kit for the prevention of an allergic disorder as claimed. The Examiner concludes that one skilled in the art would not be able to practice the invention as claimed without undue experimentation.

Applicants respectfully disagree. Nevertheless, in an effort to expedite prosecution, Applicants have amended claim 1 to recite "an isolated allergen consisting of a polypeptide capable of binding to IgE antibodies from an individual being allergic against mugwort pollen, wherein said polypeptide is selected from the group consisting of: (a) a polypeptide having an amino acid sequence that is at least 95% identical to the amino acid sequence as shown in SEQ ID NO: 1; (b) a polypeptide comprising the amino acid sequence extending between residues 21 and 180 of SEQ ID NO: 1; and (c) a polypeptide comprising the amino acid extending between residues 181 and 396 of SEQ ID NO:I." Applicants respectfully submit such amendment to claims 1 *et seq.* renders moot the Examiner's enablement concerns. To that end, Applicants direct the Examiner's attention to the enablement decision tree set forth in the "Training Materials For Examining Patent Applications With Respect To 35 USC § 112, First Paragraph - Enablement Chemical/Biotechnical Applications" first asks the question: "Does the specification teach how to make and use at least one embodiment encompassed by the claims as a whole without undue experimentation?" A note to the question states that "if there is a working example, the answer to the question cannot be 'NO'." Herein, Applicants not only provide general guidance as to how to make and use embodiments of the claimed invention but also describe at least three representative species that fall within the scope of the claimed invention (see paragraph [0016]). Accordingly, the answer to the first question is necessarily "YES".

The second question in the enablement decision tree is: "Are the enabled embodiments representative of the full scope of the claim?" As discussed in further detail below, the USPTO itself has deemed a single disclosed species to be representative of an analogous sequence variant encompassing genus. In this case, the high degree of sequence identity required by the claims yields structurally similar nucleotides; therefore, a person of skill in the art would not expect substantial variation among species within the genus. Accordingly, as Applicants have herein disclosed at least three representative species (i.e., SEQ ID NO: 1 as well as the 20-180 and 181-396 fragments thereof), the answer to this second question is necessarily "YES". Thus, following the guidelines of the enablement decision tree, no enablement rejection should be made under these circumstances. For these reasons, Applicants respectfully request reconsideration and withdrawal of the enablement rejection of claims 1-4, 15, and 18-20.

As to the Examiner's suggestion that without specific guidance as to which amino acids may be included and/or excluded, the experimentation left to those skilled in the art is undue, Applicants respectfully submit that the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, provided it is merely routine. See In re Wands 8 U.S.P.Q. 1400, 1404 (Fed. Cir. 1988). In this case, Applicants submit that the "trial and error" testing needed to identify the "core regions" protein is within the parameters of routine experimentation and optimization. Thus, Applicants submit that one of ordinary skill in the art would be able to practice the invention of the presently pending claims without undue experimentation.

As to the Examiner's assertion that Applicants' specification fails to enable *in vivo* utilities in the context of pharmaceutical applications, Applicants wish to remind the Examiner that the pending claims are directed to *compositions of matter* (i.e., allergens as well as kits, vectors, cells, and pharmaceutical compositions comprising such) and not *methods"* of using same. Accordingly, the Examiner's discussion of unpredictability and the hurdles associated with achieving *in vivo* therapeutic results are not relevant to the issue of enablement of the claimed compositions. In fact, on the issue of "how to use", section 112, first paragraph, does not require a specification to enable *all* uses of the claimed invention; rather, a single disclosed or well-established use is all that is required. Furthermore, as noted in M.P.E.P. § 2164.01(c), when a composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for non-enablement based on how to use. If multiple uses for claimed compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention. In this case, given the fact that Applicants have provided explicit working examples demonstrating the ability of the claimed embodiments to bind to IgE antibodies from subjects allergic to mugwort pollen and the diagnostic applications thereof, a rejection for lack of enablement is misplaced.

In addition, the Examiner's suggestion that "specific and detailed description" coupled with "working examples" is required seems to be in clear conflict with statutory and case law. For example, M.P.E.P. § 2107.01 and § 2107.03 clearly state that an applicant need not demonstrate that the invention is completely safe. Furthermore, under the current case law, Applicants need not prove clinical efficacy to show that a therapeutic process is operable (i.e., enabled). As stated in M.P.E.P. § 2107.01, the "courts have found utility for therapeutic inventions, despite the fact that an applicant is at a very early stage in the development of a therapeutic regimen" or that a therapeutic treatment regimen is not at a stage where it is ready to be clinically practiced. *Cross v. Iizuka,* 753 F.2d 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985); *In re Brana,* 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). The guidelines further state that "[t]he Office must confine its review of patent applications to the statutory requirements of the patent law, and in quoting *In re Brana, su___~2~_,* that "FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws". *Id.*

Rather, the patent laws merely require that a "reasonable correlation" exist between the scope of the claims and the scope of enablement. If the art is such that a particular assay or model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate. In other words, the Examiner bears the burden for providing reasons supporting her conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. Importantly, a rigorous or an invariable exact correlation is not required. See *Cross v. Iizuka,* 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985).

Thus, Applicants respectfully submit that the Examiner's allegations of a generic lack of guidance and unpredictability in the art are insufficient to support a conclusion that the presently claimed invention is not enabled for *in vivo* applications. In particular, given Applicants' conclusive demonstration that allergens of the present invention show clear and specific binding to mugwort pollen specific IgE antibodies and given that such positive *in vitro* findings are routinely correlated to positive *in vivo* findings, the burden is on the Examiner to demonstrate that one skilled in the art would not reasonably extrapolate the undisputed positive results to clinical therapy, a burden Applicants respectfully submit the Examiner has not met. Thus, Applicants submit that one of ordinary skill in the art would be able to practice the invention of the presently pending claims without undue experimentation with a reasonable expectation of success.

As to the Examiner's assertion that the instant specification fails to enable "prevention" of allergic disorders, Applicants respectfully submit that the Examiner's characterization of the term "prevent" as an absolute term is in error. According to www.wikipedia:org, "in medicine, prevention is any activity which reduces the burden of mortality or morbidity from disease". Prevention can occur "at primary, secondary and tertiary prevention levels." While "primary prevention avoids the development of a disease, secondary

> and tertiary levels of prevention encompass activities aimed at preventing the progression of a disease and the emergence of symptoms as well as reducing the negative impact of an already established disease by restoring function and reducing disease-related complications. Accordingly, Applicants respectfully submit that the term "prevent", when afforded its ordinary and customary meaning, does not necessarily equate to absolute cessation. Moreover, Applicants respectfully submit that one skilled in the art would readily recognize that, in the context of the instant claims, prevention encompasses a wide range of prophylactic therapies aimed at alleviating the onset or severity of one or more allergic symptoms. Thus, Applicants submit that one of ordinary skill in the art would be able to practice the invention of the presently pending claims without undue experimentation with a reasonable expectation of success. "

It is the Examiner's position that she has never heard of the "Training Materials For Examining Patent Applications With Respect To 35 USC § 112, First Paragraph - Enablement Chemical/Biotechnical Applications" but will address Applicant's points regarding the document to be fully responsive, though Applicant's citation is not binding precedent on any decisions.

Applicant is correct in answering the first question yes. However, Applicant is not correct in the outcome from a yes answer. The yes answer only precludes a rejection of the claims under complete lack of enablement, not a "scope of enablement" rejection as the Examiner set forth in the Office Action mailed on 08/01/2007. The Examiner would like to point Applicant's attention to " while being enabling for: an allergen consisting of SEQ ID NO:1, a composition comprising the allergen and a kit thereof, does not provide reasonable enablement for.." in the rejection. The outcome of the first question of the enablement tree is only a determination of a complete lack of enablement, not one that is simply not commensurate in scope with the claims as is the instant case.

As Examiner set forth in the Office Action mailed on 08/01/2007, the specification, including the specific embodiments, are not representative of the full scope of the claims. The Examiner is well aware that significant experimentation is not equivalent to undue experimentation. However, it is undue experimentation to determine the function of the unlimited number of polypeptides encompassed by the instant claim recitations. It is undue experimentation to determine the identity of all such polypeptides, much less to screen them for a given function. Further, as set forth in the Office Action mailed on 08/01/2007, the disclosed function may be related to the unlimited additional undisclosed additions and substitutions to the polypeptides that are encompassed by the instant claim recitations. Without specific guidance as to which amino acids may be included and/or excluded, the experimentation left to those skilled in the art is undue. Applicant's assertion that "trial and error" testing needed to identify the "core regions" of the protein is within the parameters of routine experimentation and optimization is unpersuasive. If such was the case, all inventions would be the result of routine experimentation, given sufficient time and techniques.

Applicants reference to the fact that the pending claims are directed to *compositions of matter* and not *methods"* of using same in response to the Examiner's enablement rejection with reference to in vivo and pharmaceutical use is unpersuasive. The Examiner would like to point Applicant's attention to the limitations "pharmaceutical composition" in claim 15 and "kit for the diagnosis, treatment or prevention of an allergic disorder" of claim 18. The "unpredictability and the hurdles associated with achieving *in vivo* therapeutic results" are very relevant to the patentability of the intended use of a pharmaceutical composition and a kit for treatment and prevention of disease. The fact that the "how to use", section 112, first paragraph, does not

require a specification to enable *all* uses of the claimed invention; rather, a single disclosed or well-established use is all that is required." is not relevant to the instant rejection because Applicant is claiming a "pharmaceutical composition" and a "kit for the diagnosis, treatment or prevention of an allergic disorder." As noted in M.P.E.P. § 2164.01(c), **when a composition claim is not limited by a recited use (**which is not the instant case which is limited by recited use**)**, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for non- enablement based on how to use. If multiple uses for claimed compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use (as set forth in the Office Action mailed on 08/01/2007, see pages 7-8) .

The Examiner is confused as to why Applicant argues that a specific and detailed description" coupled with "working examples" is not required to show in vivo enablement. In response to Applicant's assertion that "M.P.E.P. § 2107.01 and § 2107.03 clearly state that an applicant need not demonstrate that the invention is completely safe": the Examiner argues that she is not concerned with safety. Rather the Examiner is concerned with efficacy of the claimed invention that purports to have intended in vivo use. With respect to Applicant's assertion that "under the current case law, Applicants need not prove clinical efficacy to show that a therapeutic process is operable (i.e., enabled). As stated in M.P.E.P. § 2107.01, the "courts have found utility for therapeutic inventions, despite the fact that an applicant is at a very early stage in the development of a therapeutic regimen" or that a therapeutic treatment regimen is not at a stage where it is ready to be clinically practiced. *Cross v. Iizuka,* 753 F.2d 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985); *In re Brana,* 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995)" the

Examiner thinks the Applicant has mischaracterized the holdings in these cases. Rather, these cases show that evidence of pharmacological or other biological activity of a compound will be relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility. *Cross v. Iizuka*, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); *Nelson v. Bowler*, 626 F.2d 853, 206 USPQ 881 (CCPA 1980). In the instant case, there is no reasonable correlation between a polypeptide that binds to IgE and an in vivo treatment method for allergies as allergens cause allergy and anaphylaxis and bind IgE by definition.

Applicant's assertion that the term "prevent" is not an absolute term is in error. The term "prevent" means to keep from happening or existing. It is not a term of degree. If the thing to be "prevented" occurs, then it was not prevented. Applicant's assertion that "in medicine, prevention is any activity which reduces the burden of mortality or morbidity from disease. Prevention can occur at primary, secondary and tertiary prevention levels. While primary prevention avoids the development of a disease, secondary and tertiary levels of prevention encompass activities aimed at preventing the progression of a disease and the emergence of symptoms as well as reducing the negative impact of an already established disease by restoring function and reducing disease-related complications." actually supports the Examiner's position as Applicant's specification is directed to "primary prevention" which "avoids development of disease." Contrary to Applicant's assertion, one skilled in the art would not readily recognize that "prevention" encompasses a wide range of prophylactic therapies aimed at alleviating (not preventing) the onset or severity of one or more allergic symptoms. One of ordinary skill in the art would not recognize that prevention = non-prevention.

For the reasons set forth in the Office Action mailed on 08/01/2007 and set forth in response to Applicant's argument filed on 12/03/2007, the rejection stands.

8. Claims 1, 3-4, 15, 18, 20 and 38-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: an allergen consisting of SEQ ID NO:1; a polypeptide consisting of amino acids 181 to 396 of SEQ ID NO:1 and a polypeptide consisting of amino acids 21 to 180 of SEQ ID NO:1.

Applicant is not in possession of: an isolated allergen consisting of a polypeptide capable of binding to IgE antibodies from an individual being allergic against mugwort pollen, wherein said polypeptide is selected from the group consisting of : (a) **a polypeptide having an amino acid sequence that is at least 95% identical to the amino acid sequence as shown in SEQ ID NO: 1**; (b) **a polypeptide comprising the amino acid sequence extending between residues 21 and 180 of SEQ ID NO:1**; and (c) **a polypeptide comprising the amino acid extending between residues 181 and 396 of SEQ ID NO:1 of claim 1**; and wherein said polypeptide **comprises** the amino acid sequence as shown in SEQ ID NO: 1 of claim 3.

Applicant has disclosed only an allergen consisting of SEQ ID NO:1; a polypeptide consisting of amino acids 181 to 396 of SEQ ID NO:1 and a polypeptide consisting of amino acids 21 to 180 of SEQ ID NO:1; therefore, the skilled artisan cannot envision all the contemplated allergen possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method.

Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons

of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant's arguments filed on 12/03/2007 have been fully considered, but are not found persuasive.

Applicant argues:

> "Claims 1-4, 15, and 18-20 stand rejected under 35 U.S.C. § 112, first paragraph, for containing subject matter which was not described in such a way as to reasonably convey possession of the claimed invention. Specifically, while the Examiner accedes to Applicants' possession of an allergen consisting of SEQ ID NO: 1, she challenges whether Applicants were in possession of an allergen (a) comprising a fragment of at least 18 consecutive amino acids of the amino acid sequence shown in SEQ ID NO: 1 or (b) comprising the amino acid sequence of SEQ ID NO: 1.
>
> Applicants respectfully disagree. Nevertheless, in an effort to expedite prosecution, Applicants have amended claim 1 to recite "an isolated allergen consisting of a polypeptide capable of binding to IgE antibodies from an individual being allergic against mugwort pollen, wherein said polypeptide is selected from the group consisting of: (a) a polypeptide having an amino acid sequence that is at least 95% identical to the amino acid sequence as shown in SEQ ID NO: 1; (b) a polypeptide comprising the amino acid sequence extending between residues 21 and 180 of SEQ ID NO: 1; and (c) a polypeptide comprising the amino acid extending between residues 181 and 396 of SEQ ID NO:I. Applicants respectfully submit one of skill in the art would recognize that the Applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the presently claimed genus in view of the representative species disclosed and guidance provided in the instant specification, coupled with conventional knowledge and level of skill in the prior art.

The standard for determining compliance with the written description requirement is "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli,* 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989). The standard for determining sufficiency of the description is "factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure." *In re Wertheim,* 541 F.2d at 262 (citing *In re Ruschig* 379 F.2d 990, 995-96 (C.C.P.A. 1967)). It is well accepted that a specification may, within the meaning of 35 U.S.C. 112, first paragraph, contain a written description of a broadly claimed invention without describing all species that the claim encompasses• The law does not require that the specification describe the exact details for preparing each and every species within the genus described• In fact, even if the Examiner considers the subject matter of the claims to be broader than that disclosed in the original specification, the written description requirement may be satisfied if the broader concept would naturally occur to one skilled in the art upon reading the earlier specification.

In this case, claim 1 encompasses a genus of allergen polypeptides defined in terms of both their specific relationship to disclosed SEQ ID NO: 1 (e.g., having an amino acid sequence at least 95% identical to SEQ ID NO: 1, comprising fragment extending between residues 21 and 180 of SEQ ID NO: 1, or comprising a fragment extending between residues 181 and 396 of SEQ ID NO: 1) as well as their functional properties (e.g. "capable of binding to IgE antibodies from an individual being allergic against mugwort pollen")• Applicants respectfully submit that allowance of a claim of this scope is in line with USPTO policy regarding written description analysis as set forth the Revised Interim Written Description Guidelines published January 5, 2001, particularly the Training Materials accompanying same (see http://www.uspto.gov/web/menu/written.pdf). Specifically, the Examiner's attention is directed to Example 14 of the Training Materials which analyzes a claim directed to variants of a protein that are at least 95% identical to a particular disclosed sequence and that have a particularly specified activity. Therein, the PTO concludes that "the genus of proteins that must be variants.. • does not have substantial variation since all the variants must possess the specific catalytic activity and must have at least 95% identity to the reference sequence". Thus, "the single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provides for identifying all of the at least 95% identical variants...which are capable of the specified catalytic activity." Accordingly, "one skilled in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus" (i.e., the example claim meets the written description requirement of 35 USC § 112, first paragraph). See Training Materials, pages 53-55.

Applicants' amended claim 1 is analogous to the claim of Example 14 in that it is directed to an isolated allergen consisting of a polypeptide having at least 95% identity to

> a reference sequence, namely, SEQ ID NO: 1, and having a specifically identified function, namely the ability to bind mugwort pollen IgE antibodies. As discussed above, since the species are defined both in terms of specific structure and specific function, the genus of polypeptides encompassed by the claim will not have substantial variation. Thus, it follows that since the genus is not widely variable, only a limited number of species [e.g., SEQ ID NO: 1 as well as the 21-180 and 181-396 fragments thereof] is needed to demonstrate possession. Furthermore, Applicants' specification sets forth assays for preparing and identifying suitable polypeptides capable of performing the specified function. See, for example, paragraph [0014] (assaying IgE binding); paragraphs [0016], [0022], and [0023] (identifying and manufacturing suitable variants); and paragraphs [0006] and [0024] (determining percent identity).
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> Thus, Applicants respectfully submit that the instant specification provides an adequate written description of the genus of polypeptide allergens encompassed by claims 1 *et seq.,* so as to convey with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicants were in possession of the invention now claimed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the written description rejection of claims 1-4, *15,* and 18-20 in view of the amendments and remarks herein."

It is the Examiner's position that the specification does not disclose a correlation structure of the allergen and function (capable of binding to IgE antibodies from an individual being allergic against mugwort pollen, capable of binding to IgE antibodies from an individual being allergic against ragweed pollen) such that a skilled artisan would have known what modifications to the allergen can be made to attain the claimed function. "Possession may not be shown by merely describing how to obtain possession of member of the claimed genus or how to identify their common structural features" *Ex parte Kubin* (83 U.S.P.Q.2d 1410 (BPAI 2007)) at page 16. In this instant case Applicants have not provided any guidance as to what mutation or combination of mutations will result in the claimed functions. "Without a correlation between structure and function, the claim does little more than define the claimed invention by function" *supra*, at page 17. Further and of particular note is that the ability to bind to IgE antibodies from

an individual that is allergic to X does not require that the anti-X antibodies bind the claimed allergen.

Applicant's argument that the instant specification, sets forth a claim directed to variants of a protein that are at least 95% identical to a particular disclosed sequence and that have a particularly specified activity is not sufficient. The specification must also set forth the structural features that allow one of ordinary skill in the are to produce allergens that are capable of binding to IgE antibodies from an individual being allergic against mugwort pollen and are capable of binding to IgE antibodies from an individual being allergic against ragweed pollen. The instant applications identifies an allergen consisting of SEQ ID NO:1; a polypeptide consisting of amino acids 181 to 396 of SEQ ID NO:1 and a polypeptide consisting of amino acids 21 to 180 of SEQ ID NO:1 that have the properties called for in the instant claims, but there is no guidance on other allergens with these properties. The working examples for allergens that are capable of binding to IgE antibodies from an individual being allergic against mugwort pollen and are capable of binding to IgE antibodies from an individual being allergic against ragweed pollen are not sufficient support for the genus of all allergens encompassed by the claimed invention. In the instant case, definition by function does not suffice to define the genus because it is only an indication of what the allergen does rather than what it is.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 3-4 and 18, 20 stand rejected and claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by Nilsen et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 08/01/2007.

Applicant's arguments and declaration of Fatima Ferreira filed on 12/03/2007 have been fully considered, but are not found persuasive.

Applicant argues

> "Applicants respectfully disagree with the Examiner's characterization of the prior art disclosures. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir.1993). Rather, to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re Robertson,* 169 F.3d 743,745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Thus, in relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)
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> In this case, Applicants submit that none of the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly

described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. is identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Given the gaps in the prior art discussed in detail below and in the Rule 132 Declaration of Professor Fatima Ferreira provided herewith, Applicants submit that the evidence cited by the Examiner fails to make clear that the missing descriptive matter (i.e., the polypeptide of SEQ ID NO: 1) is necessarily present in the reference, and that it would be so recognized by persons of ordinary skill.

For example, although Nilsen et al. identified at least 15 IgE-binding components with molecular weights ranging from 12 kDa to 100 kDa, the authors provide no sequence information that would unequivocally prove that any of the isolated polypeptides is indeed identical to the polypeptide of SEQ ID NO: 1 (referred to herein as "Art v 6"). Moreover, none appear to have a molecular weight of 40,834.55 Daltons (see Figure 1 and Table 1) or a theoretical isoelectric point (pI) of 8.27 (see Figures 2-4). "

Professor Fatima Ferreira's declaration states:

"With respect to the above-referenced Nilsen publication, although Nilsen et al. identified at least 15 IgE-binding components with molecular weights ranging from 12 kDa to 100 kDa, the most prominent of which had molecular weights of 12.5, 22, and 63 kDa, the authors provide no sequence information that would unequivocally prove that any of the isolated polypeptides is indeed identical to Art v 6. Moreover, none appear to have a molecular weight of 40,834.55 Daltons (see Figure 1 and Table 1) or a theoretical isoelectric point (pI) of 8.27 (see Figures 2-4). Accordingly, I submit that none of the allergen polypeptides described by Nilsen et al. is identical to the presently claimed 40.9 kDa Art v 6 protein defined in SEQ ID NO: 1."

It remains the Examiner's position that Nilsen et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by SDS-PAGE gel (In particular, Figure 1, approximately 44 kDa bands in lanes C, E, F and K; Table 1, whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and

has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa bands of Figure 1 in Nilsen et al. are the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Applicant has not met their burden to show that the allergen in Nilsen et al. is not the allergen of SEQ ID NO:1 by saying that it does not "appear" to be the same allergen and that "no sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6." The reference need not teach the sequence to anticipate the claimed invention for reasons of record and more proof is needed than a declaration by the inventor stating that it does not "appear" to be the same protein based on a theoretical pI and molecular weight. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument is not sufficient to overcome the rejection.

11. Claims 1, 3-4 and 20 stand rejected and claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by Brandys et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 08/01/2007.

Applicant's arguments and declaration of Fatima Ferreira filed on 12/03/2007 have been fully considered, but are not found persuasive.

Applicant argues

> "Applicants respectfully disagree with the Examiner's characterization of the prior art disclosures. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir.1993). Rather, to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re Robertson,* 169 F.3d 743,745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Thus, in relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)
>
> In this case, Applicants submit that none of the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. is identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Given the gaps in the prior art discussed in detail below and in the Rule 132 Declaration of Professor Fatima Ferreira provided herewith, Applicants submit that the evidence cited by the Examiner fails to make clear that the missing descriptive matter (i.e., the polypeptide of SEQ ID NO: 1) is necessarily present in the reference, and that it would be so recognized by persons of ordinary skill.

> Likewise, while Brandys et al. observed extract band patterns in the molecular weight region of 25 kDa to 90 kDa, the authors provide no sequence information that would unequivocally prove that any of the isolated polypeptides is indeed identical to the polypeptide of SEQ ID NO: 1. Moreover, none appear to have a molecular weight of 40,834.55 Daltons (see Figure 2) or a theoretical isoelectric point (pI) of 8.27 (see Figure 3). "

Professor Fatima Ferreira's declaration states:

> "With respect to the above-referenced Brandys publication, while in the course of investigating the allergenic cross-reactivity among six mugwort (Artemisia) species, Brandys et aI. observed similar band patterns for all extracts, especiaIly in the molecular weight region of 25 kDa to 90 kDa, the authors provide no sequence information that would unequivocally prove that any of the isolated polypeptides is indeed identical to Art v 6. Moreover, none appear to have a molecular weight of 40,834.55 Daltons (see Figure 2) or a theoretical isoelectric point (pI) of 8.27 (see Figure 3). Accordingly, I submit that none of the allergen polypeptides described by Brandys et al. is identical to the presently claimed -40.9 kDa Art v 6 protein defined in SEQ ID NO: 1."

It remains the Examiner's position that Brandys et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by SDS-PAGE gel (In particular, Figure 2C, approximately 44 kDa band in lanes v, c, s, p, whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa bands of Figure 2C in Brandys et al. are the claimed allergen consisting of SEQ ID NO:1. Since

the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Applicant has not met their burden to show that the allergen in Brandys et al. is not the allergen of SEQ ID NO:1 by saying that it does not "appear" to be the same allergen and that "no sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6." The reference need not teach the sequence to anticipate the claimed invention for reasons of record and more proof is needed than a declaration by the inventor stating that it does not "appear" to be the same protein based on a theoretical pI and molecular weight. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument is not sufficient to overcome the rejection.

12. Claims 1, 3-4 and 20 stand rejected and claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by Hirschwehr et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 08/01/2007.

Applicant's arguments and declaration of Fatima Ferreira filed on 12/03/2007 have been fully considered, but are not found persuasive.

Applicant argues

> "Applicants respectfully disagree with the Examiner's characterization of the prior art disclosures. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir.1993). Rather, to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re Robertson,* 169 F.3d 743,745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Thus, in relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)
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> In this case, Applicants submit that none of the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. is identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Given the gaps in the prior art discussed in detail below and in the Rule 132 Declaration of Professor Fatima Ferreira provided herewith, Applicants submit that the evidence cited by the Examiner fails to make clear that the missing descriptive matter (i.e., the polypeptide of SEQ ID NO: 1) is necessarily present in the reference, and that it would be so recognized by persons of ordinary skill.
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> With respect to the Hirschwehr publication, while the authors identified a number of allergenic structures common in mugwort and ragweed pollen, they provide no sequence information that would unequivocally prove that any of the isolated polypeptides is indeed identical to the polypeptide of SEQ ID NO: 1. Moreover, none appear to have a molecular weight *of 40,834.55* Daltons (see Figures 1-3) or a theoretical isoelectric point (pI) of 8.27 (not shown)."

Professor Fatima Ferreira's declaration states:

> "With respect to the above-referenced Hirschwehr publication, while Hirschwehr et al. identified a number of allergenic structures common in mugwort and ragweed pollen, the authors provide no sequence information that would unequivocally prove that any of the isolated polypeptides is indeed identical to Art v 6. Moreover, none appear to have a molecular weight of 40,834.55 Daltons (see Figures 1-3) or a theoretical isoelectric point (pI) of 8.27 (not shown). Accordingly, I submit that none of the allergen polypeptides described by Hirschwehr et al. is identical to the presently claimed -40.9 kDa Art v 6 protein defined in SEQ ID NO: 1."

It remains the Examiner's position that Hirschwehr et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by SDS-PAGE gel (In particular, approximately 44kDa bands in Figure 1A, bands in lanes 10, 11 and 13; Figure 3A, lanes 6 and 7; and Figure 5, patients A and B; whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa bands of Figures 1A, 3A and 5 in Hirschwehr et al. are the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Applicant has not met their burden to show that the allergen in Hirschwehr et al. is not the allergen of SEQ ID NO:1 by saying that it does not "appear" to be the same allergen and that "no sequence information is

provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6." The reference need not teach the sequence to anticipate the claimed invention for reasons of record and more proof is needed than a declaration by the inventor stating that it does not "appear" to be the same protein based on a theoretical pI and molecular weight. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument is not sufficient to overcome the rejection.

13. Claims 1, 3-4 and 20 stand rejected and claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by De La Hoz et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 08/01/2007.

Applicant's arguments and declaration of Fatima Ferreira filed on 12/03/2007 have been fully considered, but are not found persuasive.

Applicant argues

> "Applicants respectfully disagree with the Examiner's characterization of the prior art disclosures. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir.1993). Rather, to

establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re Robertson,* 169 F.3d 743,745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Thus, in relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)

In this case, Applicants submit that none of the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. is identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Given the gaps in the prior art discussed in detail below and in the Rule 132 Declaration of Professor Fatima Ferreira provided herewith, Applicants submit that the evidence cited by the Examiner fails to make clear that the missing descriptive matter (i.e., the polypeptide of SEQ ID NO: 1) is necessarily present in the reference, and that it would be so recognized by persons of ordinary skill.

With respect to the de la Hoz publication, Applicants respectfully submit that the authors' designation of the purified mugwort allergen as "Art v 1" is incorrect. In any event, the authors provide no sequence information that would unequivocally prove that the isolated polypeptide is indeed identical to the polypeptide of SEQ ID NO: 1. Furthermore, since under native conditions the protein was estimated to be 47,000 Da and under denaturing (SDS-PAGE) it was estimated to be 60,000 Da, the real molecular weight of the purified "Art v 1" protein is not known. In contrast, the polypeptide of SEQ ID NO: 1 (Art v 6) has a calculated molecular weight of 40,834.55 Da and under denaturing conditions (SDS-PAGE) it migrates as a 40,000 Da protein (see Figure 5 of the instant application). In addition, while analytical isoelectric focusing showed that the protein isolated by de la Hoz et al. is an acidic protein having a pI of 4.4, the polypeptide of SEQ ID NO: 1 is a basic protein with a pI of 8.2."

Professor Fatima Ferreira's declaration states:

"With respect to the above-referenced de la Hoz publication, de la Hoz et al. describe the purification of a mugwort allergen which was incorrectly designated as "Art v 1". However, the authors provide no sequence information that would unequivocally prove that the isolated polypeptide is indeed identical to Art v 6. Furthermore, since under native conditions the protein was estimated to be 47,000 Da and under denaturing (SDS-PAGE) it was estimated to be 60,000 Da, the real

> molecular weight of the purified "Art v 1" protein is not known. In contrast, Art v 6 has a calculated molecular weight of 40,834.55 Da and under denaturing conditions (SDS-PAGE) it migrates as a 40,000 Da protein (see Figure 5 of the instant application). In addition, while analytical isoeleetric focusing showed that the protein isolated by de la Hoz et al. is an acidic protein having a pI of 4.4, Art v 6 is a basic protein with a pI of 8.2. Accordingly, I submit that the "Art v 1" protein described by de la Hoz is not identical to the presently claimed -40.9 kDa Art v 6 protein defined in SEQ ID NO: 1."

It remains the Examiner's position that De La Hoz et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by SDS-PAGE gel (In particular, approximately 44kDa bands in Figure 3, lanes A and B, Figure 4, lanes A, B and C; whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa bands of Figure 3 in De La Hoz et al. are the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Applicant has not met their burden to show that the allergen in De La Hoz et al. is not the allergen of SEQ ID NO:1 by saying that it does not "appear" to be the same allergen and that

"no sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6." The reference need not teach the sequence to anticipate the claimed invention for reasons of record and more proof is needed than a declaration by the inventor stating that it does not "appear" to be the same protein based on a theoretical pI and molecular weight. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument is not sufficient to overcome the rejection.

14. Claims 1, 3-4, 18 and 20 stand rejected and claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by Katial et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 08/01/2007.

Applicant's arguments and declaration of Fatima Ferreira filed on 12/03/2007 have been fully considered, but are not found persuasive.

Applicant argues:

> "Applicants respectfully disagree with the Examiner's characterization of the prior art disclosures. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir.1993). Rather, to

establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re Robertson,* 169 F.3d 743,745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Thus, in relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)

In this case, Applicants submit that none of the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al. or Paulsen et al. is identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Given the gaps in the prior art discussed in detail below and in the Rule 132 Declaration of Professor Fatima Ferreira provided herewith, Applicants submit that the evidence cited by the Examiner fails to make clear that the missing descriptive matter (i.e., the polypeptide of SEQ ID NO: 1) is necessarily present in the reference, and that it would be so recognized by persons of ordinary skill.

With respect to the Katial publication, while the authors utilized ELISA and IgE immunoblots to investigate cross-reactivity among mugwort *(Artemisia)* species, they provide no sequence information that would unequivocally prove that any of the isolated polypeptides is indeed identical to the polypeptide of SEQ ID NO: 1. In addition, while Katial et al. describe IgE-binding peptides in all extracts in the 66-kDa, 45-kDa, and 21-kDa ranges, they fail to specifically mention an IgE-binding protein in the range of 40-kDa."

Professor Fatima Ferreira's declaration states:

"With respect to the above-referenced Katlal publication, Katial et al. utilized ELISA and IgE immunoblots to investigate cross-reactivity among mugwort (Artemisia) species. However, the authors provide no sequence information that would unequivocally prove that any of the isolated polypeptides is indeed identical to Art v 6. In addition, while Katial et al. describe IgE-binding peptides in all extracts in the 66-kDa, 45-kDa, and 21-kDa ranges, they fail to specifically mention an IgE-binding protein in the range of 40-kDa. Accordingly, I submit that none of the allergen polypeptides described by Katial et al. is identical to the presently claimed -40.9 kDa Art v 6 protein defined in SEQ ID NO: 1."

It remains the Examiner's position that Katial et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by SDS-PAGE gel (In particular, Figure 5, approximately 44kDa band in lane AV; whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa band of Figure 5 in Katial et al. is the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Applicant has not met their burden to show that the allergen in Katial et al. is not the allergen of SEQ ID NO:1 by saying that it does not "appear" to be the same allergen and that "no sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6." The reference need not teach the sequence to anticipate the claimed invention for reasons of record and more proof is needed than a declaration by the inventor stating that it does not "appear" to be the same protein based on a theoretical pI and molecular weight. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. The Examiner has

asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument is not sufficient to overcome the rejection.

15. Claims 1, 3-4, 15, 18 and 20 stand rejected and claim 38 is rejected are rejected under 35 U.S.C. 102(b) as being anticipated by Paulsen et al. (of record) as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) for the same reasons as set forth in the Office Action mailed on 08/01/2007.

Applicant's arguments and declaration of Fatima Ferreira filed on 12/03/2007 have been fully considered, but are not found persuasive.

Applicant argues:

> "Applicants respectfully disagree with the Examiner's characterization of the prior art disclosures. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert,* 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir.1993). Rather, to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re Robertson,* 169 F.3d 743,745, 49 USPQ2d 1949, 1950-51 (Fed. Cir.1999). Thus, in relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Exparte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)
>
> In this case, Applicants submit that none of the "approximately 44 kDa polypeptide allergens isolated from mugwort pollen using SDS-PAGE gel" allegedly described by Nilsen et al., Brandys et al., Hirschwehr et al., de la Hoz et al., Katial et al.

> or Paulsen et al. is identical to the presently claimed polypeptide of SEQ ID NO: 1, referred to in Gen Bank Accession Number AY904433 as "Art v 6". Given the gaps in the prior art discussed in detail below and in the Rule 132 Declaration of Professor Fatima Ferreira provided herewith, Applicants submit that the evidence cited by the Examiner fails to make clear that the missing descriptive matter (i.e., the polypeptide of SEQ ID NO: 1) is necessarily present in the reference, and that it would be so recognized by persons of ordinary skill.
>
> With respect to the Paulsen publication, while the disclosed results indicate the presence of proteins in the MW region of 20,000-70,000, since no further purification of the individual components of the complex mixture or IgE-binding tests was performed, it cannot be said with any certainty whether any of the disclosed components are allergenic. In any event, the amino acid analysis of Paulsen's crude extract yields an amino acid composition that is quite distinct from that of the polypeptide of SEQ ID NO: 1 (see the amino acid content comparison set forth in Appendix B, attached hereto)."

Professor Fatima Ferreira's declaration states:

> "With respect to the above-referenced Paulsen publication, Paulsen et al. describe the extraction of allergens from mugwort pollen using two different buffer systems, phosphate-buffered saline or NH4HCO3. Gel filtration of the NH4HCO3 extract indicated the presence of proteins in the MW region of 20,000-70,000. The extract represents a complex mixture of different proteins. Since no further purification of the individual components and IgE-binding tests were performed, it cannot be said with any certainly whether the disclosed components are allergenic. In any event, the amino acid analysis of Paulsen's crude extract yields an amino acid composition that is quite distinct from that of Art v 6 (see the amino acid content comparison set forth in Appendix B, attached hereto). Accordingly, I submit that none of the polypeptides described by Paulsen et al. is identical to the presently claimed -40.9 kDa Art v 6 protein defined in SEQ ID NO: 1."

It remains the Examiner's position that Paulsen et al. identifies an approximately 44 kDa polypeptide allergen in mugwort (Artemisia vulgaris) pollen by gel permeation chromatography (In particular, Figure 6 A and B, approximately 45kDa fractions; 'Gel Permeation Chromatography' section on page 207; Table 1; whole document). Genbank Accession Number AY904433 and http://www.allergen.org/Allergen.aspx are being used as an evidentiary

references to show that the protein of SEQ ID NO:1 is called 'Art v 6' and has a molecular weight of approximately 44kDa on SDS-PAGE. Those of ordinary skill in the art recognize that discrepencies are often encountered in the art between protein molecular weights when determined by different methods. The broadest reasonable interpretation of the claims reads on the reference protein. Therefore, absent evidence to the contrary, the approximately 44 kDa fraction of Figure 6A and 6B in Paulsen et al. is the claimed allergen consisting of SEQ ID NO:1. Since the office does not have a laboratory to test the reference allergen, it is applicant's burden to show that the reference allergen is not the allergen recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980). Applicant has not met their burden to show that the allergen in Paulsen et al. is not the allergen of SEQ ID NO:1 by saying that it does not "appear" to be the same allergen and that "no sequence information is provided to unequivocally prove that any of the isolated polypeptides is indeed identical to At v 6." The reference need not teach the sequence to anticipate the claimed invention for reasons of record and more proof is needed than a declaration by the inventor stating that it does not "appear" to be the same protein based on a theoretical pI and molecular weight. It is the Examiner's position that the reference protein is the protein of SEQ ID NO:1 because it is an allergen that binds to IgE from allergic patients and it has been isolated from mugwort pollen, just like the protein of SEQ ID NO:1. The Examiner has asked Applicant to prove that it is not the same protein because the Patent Office does not have a laboratory to test the reference protein. However, Applicant's evidence and argument is not sufficient to overcome the rejection.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claim 19 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsen et al. (of record), Brandys et al. (of record), Hirschwehr et al. (of record), De La Hoz et al. (of record), Katial et al. (of record), **or** Paulsen et al. (of record) each as evidenced by http://www.allergen.org/allergen.aspx (of record) and GenBank Accession Number AY904433 (of record) each in view of U.S. Patent 4,459,360 (of record) for the same reasons as set forth in the Office Action mailed on 08/01/2007.

Applicant's arguments and declaration of Fatima Ferreira filed on 12/03/2007 have been fully considered, but are not found persuasive.

Applicant argues:

> "Applicants respectfully submit that US '360 fails to cure the above-noted deficiencies of the Nilsen, Brandys, Hirschwehr, De La Hoz, Katial, and Paulsen references, namely the disclosure of an -40.9 kDa "Art v 6" protein defined by SEQ ID NO: 1. Thus, in that the prior art references, alone or in combination, fail to teach or suggest all the claim limitations, Applicants respectfully submit that the Examiner has

> failed to set forth a *prima facie* case of obviousness. Accordingly, Applicants respectfully request reconsideration and withdrawal of the obviousness rejection of claim 19 in view of the amendments and remarks herein."

It remains the Examiner's position that Nilsen et al., Brandys et al., Hirschwehr et al., De La Hoz et al. and Katial et al. teach the protein of SEQ ID NO:1 for the reasons set forth in the Office Action mailed on 08/01/2007 and for the arguments set forth *supra*. It also remains the Examiner's position that it would have been obvious to one of ordinary skill in the art at the time of invention to use the isolated allergen fraction of Paulsen et al. or the isolated allergen band of Nilsen et al., Brandys et al., Hirschwehr et al., De La Hoz et al. or Katial et al. in a diagnostic kit for allergy screening for that allergen as taught by the '360 Patent because the '360 Patent teaches that such a kit would be economical, easy to analyze and useful as an allergy screening system.

18. No claim is allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

February 29, 2008
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/Maher M. Haddad/
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